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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 316

[Docket No. FDA-2011-N-0583]

Clarification of Orphan-Drug Exclusivity Following *Catalyst Pharms., Inc*. v. *Becerra*; Notification

AGENCY: Food and Drug Administration, Department of Health and Human Services (HHS).

ACTION: Notification.

SUMMARY: The Food and Drug Administration (FDA or Agency) is publishing this notification in light of the recent decision by the U.S. Court of Appeals for the Eleventh Circuit in *Catalyst Pharms., Inc.* v. *Becerra*. The *Catalyst* decision addressed the orphan-drug exclusivity provision of the Federal Food, Drug, and Cosmetic Act (FD&C Act), as amended by the Orphan Drug Act and subsequent amendments, and concluded that FDA's approval of Jacobus Pharmaceutical Company's (Jacobus's) drug (the drug at issue in the litigation) must be set aside. Consistent with the court's decision, FDA has set aside its approval of Jacobus's drug. This notification announces that, at this time, while complying with the court's order in *Catalyst*, FDA intends to continue to apply its regulations tying the scope of orphan-drug exclusivity to the uses or indications for which a drug is approved to matters beyond the scope of that order.

DATES: The policy set out in this document is effective [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

FOR FURTHER INFORMATION CONTACT: Aaron Friedman, Office of Orphan Products Development, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993, 301-796-2989.

SUPPLEMENTARY INFORMATION:

I. Background

On September 30, 2021, the U.S. Court of Appeals for the Eleventh Circuit issued a decision in *Catalyst Pharms., Inc.* v. *Becerra* (*Catalyst*), 14 F.4th 1299 (11th Cir. 2021).

At the time of the litigation, Jacobus and Catalyst Pharmaceuticals (Catalyst) each had orphan-drug designation for the drug amifampridine for the treatment of Lambert-Eaton myasthenic syndrome (LEMS). In November 2018, FDA approved Catalyst's drug for the treatment of LEMS in adults. FDA recognized Catalyst's drug as eligible for orphan-drug exclusivity for its only approved indication--the treatment of LEMS in adults.

In May 2019, FDA approved Jacobus's drug for the treatment of LEMS in children. In approving Jacobus's drug, FDA followed its longstanding rule, codified in its regulations, that the orphan-drug exclusivity for Catalyst's drug protected only the approved use or indication within the designated disease. *See* 21 CFR 316.3(b)(12), 316.31(a)-(b). The regulation in 21 CFR 316.31(b) states, in part, that: "Orphan-drug exclusive approval protects *only the approved indication or use of a designated drug*."[1]

In June 2019, Catalyst filed suit against FDA, challenging FDA's approval of Jacobus's application under the Administrative Procedure Act, 5 U.S.C. 701-706. Among other things, Catalyst argued that the phrase "same disease or condition" in the Orphan Drug Act, 21 U.S.C. 360cc(a), unambiguously prohibited FDA from approving Jacobus's drug application. Specifically, Catalyst argued that the Orphan Drug Act required orphan-drug exclusivity to extend to *all* uses or indications within the orphan-designated disease or condition--even uses or

[1] Emphasis added. Other regulatory provisions also reflect the understanding that orphan-drug exclusivity is tied to the use or indication for which the drug was approved. *See* § 316.3(b)(12) (stating that "no approval will be given to a subsequent sponsor of the same drug for the *same use or indication* for 7 years" (emphasis added)); *see also id.* § 316.31(a) (explaining that FDA may approve an orphan drug for "select *indication(s) or use(s)* within the rare disease or condition for which the drug was designated" and that "FDA will not approve another sponsor's marketing application for the same drug for the *same use or indication* before the expiration of 7 years from the date of such approval" (emphases added)).

indications for which Catalyst had not received approval, such as the treatment of LEMS in children.

The district court rejected Catalyst's argument that the Orphan Drug Act required orphan-drug exclusivity to apply to all uses or indications within the orphan-designated disease or condition. The district court concluded that, given the context and the overall statutory scheme, the statute was ambiguous on the disputed issue, and that FDA had reasonably interpreted the statute to tie orphan-drug exclusivity to the uses or indications for which the drug was approved.

On appeal, the U.S. Court of Appeals for the Eleventh Circuit reversed. The circuit court concluded that the phrase "same disease or condition" in the Orphan Drug Act, 21 U.S.C. 360cc(a), unambiguously foreclosed FDA's interpretation of the provision. Accordingly, the circuit court held that orphan-drug exclusivity for Catalyst's drug blocked FDA's approval of Jacobus's drug for *all* uses or indications within the orphan-designated disease (LEMS)--even though Catalyst's drug was approved at that time only for use in the treatment of LEMS in adults. The court concluded that FDA's approval of Jacobus's drug for the treatment of LEMS in children must be set aside. Consistent with the court's decision, the Agency set aside the approval of Jacobus's drug.

II. Orphan-Drug Exclusivity

The Agency is issuing this statement to address the uncertainty created by the circuit court's decision in *Catalyst*. The court ordered FDA to set aside its approval of Jacobus's drug, and FDA has set aside that approval. This notification announces that, at this time, in matters beyond the scope of that court order, FDA intends to continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved. The Agency believes that this approach is appropriate for several reasons. FDA continues to believe that the statutory text does not unambiguously require that orphan-drug exclusivity extend to the entire disease or condition for which a drug received orphan-drug designation if the drug is only approved for some uses within that disease or condition. Further, FDA believes that

its statutory interpretation embodied in its regulations best advances the Orphan Drug Act's purposes, appropriately balancing the need to incentivize the development of drugs for rare diseases and conditions with the need to provide patient access to orphan drugs. The regulations accomplish this by tying the scope of orphan-drug exclusivity to only the approved use or indication of the drug, which permits other sponsors to obtain approval of the drug for uses or indications within the same orphan-designated disease or condition that have not yet been approved (i.e., that are "new"). Under the regulations, a drug approved for a new use or indication within the same orphan-designated disease or condition may also be eligible for orphan-drug exclusivity for such use or indication. These regulations incentivize sponsors to continue to develop a drug for use in all persons affected by a rare disease or condition. Thus, FDA believes that continued adherence to its validly promulgated regulations will best serve the public health by facilitating patient access to orphan drugs, especially for difficult-to-study patients such as young children.

III. Conclusion

For the above reasons, at this time, the Agency intends to continue to apply its longstanding regulations tying the scope of orphan-drug exclusivity to the uses or indications for which the orphan drug was approved.

Dated: January 18, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

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